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57. (Amended) The biologically active, heteromultimeric polypeptide fusion of claim 56 wherein one of said receptor domains comprises a ligand binding domain.

58. (Amended) The biologically active, heteromultimeric polypeptide fusion of claim 45 which is a heterotetramer comprising four polypeptide fusions each having a non-immunoglobulin polypeptide joined to a multimerizing protein.

REMARKS

With entry of this amendment, claims 29-43 and 45-58 are pending in the Application. By this amendment, claim 44 has been canceled, as the subject matter of this claim is embodied elsewhere in the pending claims as amended herein. Claims 29-43 and 45-58 have been amended for clarity in accordance with the Examiner's suggestions. All of the amendments presented herein are fully supported by the specification and no new matter has been added to the application. Entry of this amendment is respectfully requested.

Information Disclosure Statement

The Office reports that three references cited in the IDS submitted in the present applications were missing from the parent applications at the time the current application was abandoned. Applicants submit herewith copies of the three references, BD (Ellis et al.), CK (Struhl et al.), and CL (Broach et al.) as suggested by the Office. The Office states that these references will be considered as part of the Original IDS submitted prior to the first action on the merits (Office Action at page 2, paragraph 3).

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Formal Requirements

Claim 39 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, claim 37. This objection is overcome by the amendment to claim 37 herein to clarify and recast the subject matter of the claim in independent form.

Claim 36 has been amended in accordance with the Office's suggestion. Applicants have also amended claim 43 to correct a lack of antecedent basis for the term "mutimerizing protein".

Double Patenting

Claims 29-36, 45-53 and 55-57 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-9 of U.S. Patent No. 5,750,375. Claims 29-31, 35 and 36 are provisionally rejected for obviousness-type double patenting over claim 1 of U.S. Patent No. 5,155,027. Lastly, claims 29-58 are provisionally rejected for obviousness-type double patenting over claims 1-49 of copending application Serial No. 08/475,458 (now issued as U.S. Patent No. 5,843,725).

All of the above-identified double patenting rejections are overcome by the terminal disclaimer filed herewith. This disclaimer is filed solely to advance the application to issuance, and Applicants do not acquiesce to the merits of the imposed double patenting rejections. Thus, Applicants reserve the right to distinguish the inventions set forth in the subject claims.

Patentability Under 35 U.S.C. § 112

The specification stands objected to and claims 45 and 46 and dependent claims 47-58 rejected under 35 U.S.C. § 112, second paragraph. In particular, the Office asserts that recitation of amino acid sequences in claim 46 by reference to

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figures setting forth both amino acid and nucleic acid sequences is indefinite. While Applicants submit that no indefiniteness arises in this context, the claim has been amended for clarity as suggested by the Office to obviate the stated objection.

With respect to claim 45, the Office objects to the language "heteromultimeric polypeptide fusion" on the basis that the claim does not specify which part(s) of the fusion makes the polypeptide a heteromultimer as opposed to a homomultimer. Applicants respectfully submit that the claim in question clearly conveys the subject matter of the invention. In particular, one skilled in the art will readily understand that polypeptides requiring dimerization for biological activity include both homodimers and heterodimers. With specific regard to heteromultimers, the claimed polypeptide fusions can be heteromultimeric as a result of different multimerizing proteins (e.g., a multimer comprising immunoglobulin heavy and light chain constant regions), or different non-Ig polypeptides. Thus, the subject matter of the claims is reasonably distinct.

Claims 37 and 39-44 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly incomplete for omitting essential elements. More specifically, the Office contends that the recited components "do not form a multimerizing polypeptide fusion because nothing multimerizes with the non-Ig polypeptide." Applicants respectfully traverse and submit that all essential components are set forth in the claim. In particular, the specification clearly discloses that, for example, the recited immunoglobulin light chain constant region is a multimerizing protein. As set forth in the subject claims, nothing is required to multimerize per se to the non-Ig polypeptide, but instead multimerization can occur with an immunoglobulin light chain constant region to which the non-Ig polypeptide is joined.

Claims 29-58 stand rejected under 35 U.S.C. § 112, second paragraph. In particular, the Office contends that the

claims are not directed to the subject matter which Applicants regard as their invention because they do not recited that the subject polypeptide fusions are "secreted" and "biologically active."

Although Applicants believe that the original claims clearly set forth the subject matter of the invention, the claims have nonetheless been amended herein for clarity to recite that the subject polypeptide fusions are "biologically active." The claims have not been amended to include the term "secreted," as this term has no limiting significance with respect to the claimed polypeptide fusions. On the contrary, the term "secreted" merely refers to a process limitation, and the subject claims are not product-by-process claims. Moreover, a requirement for recitation of the term "secreted" would be inconsistent with the Office's assertion at page 4 of the Office Action, paragraph 8, that "the currently claimed dimerized, multimerized, and heteromultimerized polypeptide fusions cannot be produced by a means other than the method of the patented claim" (which patented claims recite secretion).

Priority

The Office contends that application 07/347,291, filed 05/02/89 fails to disclosed the concept of multimerized or heteromultimerized polypeptide fusions as presently claimed, whereby the priority for this aspect of the present invention is allegedly assigned to application 07/634,510, filed 12/27/90. Applicants respectfully disagree.

The '291 application clearly discloses the concept of multimerized or heteromultimerized polypeptide fusions-- throughout the specification. Specific examples are provided, for example, in Example 12C (PDGF receptor-light chain fusion co-expressed with heavy chain), Example 12E (PDGF receptor-heavy chain fusion co-expressed with light chain), and Example 12F (co-

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expression of heavy and light chain sequences each fused to PDGF receptor sequences). Additional examples are disclosed in 12G and 12H. Appropriate recognition of priority for multimerized and heteromultimerized polypeptide fusions extending to the '291 application is therefore earnestly solicited.

Patentability Under 35 U.S.C. § 102

Claims 37-45, 47-55 and 58 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Capon et al. Applicants respectfully traverse.

The cited Capon et al. reference is clearly not entitled to its earliest claimed priority date for the teachings attributed to it by the Office. On the contrary, the Capon et al. priority case, Serial No. 07/315,015 (courtesy copy enclosed), merely discloses fusion of a single receptor, lymphocyte homing receptor or LHR, to immunoglobulin chains or fragments thereof for the purpose of enhancing plasma half-life. [see, page 13 at lines 4-35]. The instant claims 37-45, 47-55, and 58 are fully supported by the priority application serial No. 07/347,291, filed May 2, 1989, as noted above. The following is a non-limiting, exemplary table showing support for each of the subject claims within the '291 specification.

<u>Claim</u>	<u>Support in '291</u>
37	p. 22, line 19 - p. 23, line 10; p. 65, line 1 - p. 67, line 5
38	p. 69, lines 1 - 15
39	p. 22, lines 10 - 18; lines 32 - 35
40	p. 22, lines 10 - 18
41	p. 22, lines 10 - 15; p. 69, line 17 - p. 70, line 21
42	p. 23, lines 12 - 13
43	p. 23, lines 7 - 13
44	p. 22, line 19 - p. 23, line 10; p. 65, line 1 - p. 67, line 5
45	p. 69, lines 1 - 15
47	p. 69, lines 1 - 15
48	p. 69, lines 1 - 15

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49 p. 69, lines 1 - 15
50 p. 69, lines 1 - 15
51 p. 69, lines 1 - 15
52 p. 67, lines 8 - 12; p. 69, lines 1 - 15
53 p. 22, lines 12 - 15
54 p. 23, lines 12 - 13
55 p. 23, lines 7 - 10
56 p. 69, lines 1 - 15

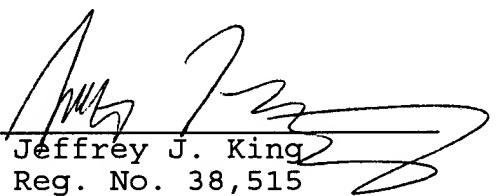
In light of Applicants' clear priority and the deficiencies of the Capon et al. priority disclosure, the rejection of claims 37-45, 47-55 and 58 under 35 U.S.C. § 102(b) is believed to be overcome.

In view of the above amendments to the claims and accompanying remarks, Applicants believe that each rejection has been addressed and overcome and that the application is now in condition for allowance. Notice to that effect is requested. If for any reason, however, the Examiner feels that a telephone conference would expedite prosecution of the subject application, the Examiner is invited to telephone the undersigned at 206/467-9600.

Respectfully submitted,

Dated: 3/28/99

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